

### **Remarks**

Claims 1-4 and 21-24 are pending in the application. Claims 1-4 stand rejected, and claims 21-24 have been withdrawn from consideration by the Examiner. Claims 1 and 4 have been amended. New claim 25 has been added. Support for claim 25 can be found in original claim 3. Applicant submits that new matter is added by these amendments. Applicant respectfully requests reexamination and reconsideration of the case in light of the following remarks. Each of the rejections levied in the Office Action is addressed individually below.

**I. Claim objections.** Claim 1 has been objected to by the Examiner for including non-elected subject matter. The Examiner has suggested that the claim be amended to include only Wnt5a and that the other twenty genes listed in the claim be removed. Unfortunately, such an amendment is not possible because deleting the other listed genes would not allow the claim to cover the invention of the Applicant.

As discussed in the Response to the Restriction Requirement filed July 21, 2003, the invention is not just determining the expression of one gene out of twenty-one in order to identify a tumor as aggressive or non-aggressive. Instead, the invention involves determining the expression of a combination of the listed genes (that is, a subset) to identify an aggressive or non-aggressive tumor. The breadth of protection necessary for adequate protection of the inventor's contribution to the art must include a claim listing all twenty genes. Given the Restriction Requirement and the Examiner's objection, Applicant has amended claim 1 to include analyzing for the expression of Wnt5a and at least one gene selected from the other nineteen genes listed in the claim. As claim 1 stands now, Wnt5a expression would always be analyzed and the other gene(s) to be analyzed could be selected from the list of twenty genes by one of skill in the art practicing the invention. Applicant requests that the objection to claim 1 be removed in light of the current amendment and the contribution of the inventors to the art in selecting these twenty genes out of approximately 7,000 unique genes examined by the inventors (see page 21, line 16).

**II. Rejection under 35 U.S.C. § 112, second paragraph.** Claims 1-4 have been rejected by the Examiner under 35 U.S.C. § 112, second paragraph, for failing to particularly point out and

distinctly claim the subject matter which Applicant regards as the invention. The Examiner maintains that “it is not clear how the expression pattern provides a nexus for determining whether or not the tumor is aggressive or nonaggressive.” However, in the next sentence, the Examiner states that “[t]he specification teaches (page 51) that melanoma samples with high levels of Wnt5a expression were more aggressive tumors than those with lower levels.” Thus, the Examiner explicitly acknowledges the nexus, defined in the Specification, between gene expression pattern and tumor aggressiveness. Applicant, therefore, submits that the claims as written in light of the specification are not indefinite to one of skill in the art reading the application, and Applicant requests that the rejection be removed.

Claims 1-3 have also been rejected for reciting “analyzing a set of genes” in conjunction with the Markush group of alternative genes. Applicant has amended claim 1 to recite “analyzing expression of Wnt5a and at one least one gene selected from the group consisting of . . .” Applicant submits that the amendment renders the Examiner’s rejection moot.

**III. Rejection under 35 U.S.C. § 102(b), as being anticipated by Iozzo *et al.*** Claim 1 and 3-4 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Iozzo *et al.*, *Cancer Research* 55:3495-99, 1995. The Examiner states that “Iozzo *et al.* teach a method of diagnosing a form of cancer comprising providing a genetic sample from a test sample of a tumor and analyzing expression of the Wnt5a gene wherein the cancer is a malignant melanoma.” Although Iozzo *et al.* may teach analyzing for Wnt5a expression, Iozzo *et al.* does not teach analyzing for any of the other genes recited in claim 1. Since Iozzo *et al.* do not teach the analysis for any other gene besides Wnt5a, they can not anticipate claims 1 and 3.

In addition, claim 4 has been amended to include the step of selecting a treatment regimen. Such a step is not disclosed by Iozzo *et al.*; therefore claim 4 is not anticipated by Iozzo *et al.* Applicant, therefore, requests that the rejection be removed.

**IV. Rejection under 35 U.S.C. § 103(a), as being unpatentable over Iozzo *et al.*** Claims 1-4 have been rejected by the Examiner under 35 U.S.C. § 103(a), as being unpatentable over Iozzo *et al.*, *Cancer Research* 55:3495-99, 1995. The Examiner states that Iozzo *et al.* teach the analysis for Wnt5a expression and that it would have been obvious that diagnosis with an

aggressive or a non-aggressive tumor would require the clinician to present the patient with some type of treatment option to lower the risk of mortality.

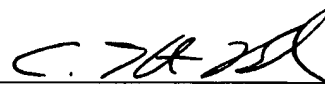
With respect to claims 1-3, Iozzo *et al.* do not teach or suggest the analysis for any of the other genes listed. Since the cited art does not teach or even suggest the analysis of expression of any of the other nineteen genes listed, it can not render obvious the claimed invention of claims 1-3. Applicant, therefore submits that the rejection be removed.

With respect to claim 4, even though a clinician may be required to present a patient with a treatment option whether the tumor is aggressive or not, the cited art does not teach that the treatment options for an aggressive tumor may be different than the treatment options for a non-aggressive tumor. In addition, an aggressive tumor expressing Wnt5a may be treated with an agent known to inhibit Wnt5a activity in order to lessen the chance of local spread or metastasis. Iozzo *et al.* do not teach or suggest that a different treatment be given for a tumor expressing Wnt5a versus a tumor found to not express Wnt5a. Given the deficiency in Iozzo *et al.*, Applicant requests that the rejection be removed.

In view of the forgoing amendments and arguments, Applicant respectfully submits that the present case is now in condition for allowance. A Notice to that effect is requested.

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Respectfully submitted,



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